

IN THE SPECIFICATION:

Please amend the specification as shown:

Please delete the paragraph on page 3, lines 13-19, and replace it with the following paragraph:

The 336-351 peptide used to prepare a conjugate in accordance with the present invention has the following amino acid sequence :-

QPHDLGKVGIVTKD (SEQ ID NO: 1)

The corresponding peptide from HSP65 (residue numbers 311-326) has the sequence :-

DLSLLGKARKVVVTKD (SEQ ID NO: 2)

This peptide may be used as an alternative to the HSP60 336-351 peptide.

Please delete the paragraph on page 3, lines 21-23, and replace it with the following paragraph:

For greater ease of conjugation we have added an N-terminal cysteine residue and a C-terminal acetate group to the above sequence to give:-

CQPHDLGKVGIVTKD-acetate (SEQ ID NO: 3).

Please delete the paragraph on page 7, line 15, to page 9, line 2, and replace it with the following paragraph:

All patients were HLA typed, as described before (1997 Tissue Antigens 50:100-111).

1. Preparation of GMP peptide 336-351 covalently linked to human HSP60

The BD peptide corresponding to residues 336-351 of the human HSP60 and with an N-terminal Cys residue was synthesized in its acetate form under GMP conditions (H-Cys-Gln-Pro-His-Asp-Leu-Gly-Lys-Val-Gly-Glu-Val-Ile2-Val-Thr-Lys-AspOH acetate **(SEQ ID NO: 3)**) by Bachem (Bachem AG, Bubendorf, Switzerland).

This peptide was coupled to a highly purified, recombinant CTB (rCTB) produced under GMP by SBL Vaccine (Stockholm, Sweden), commonly used as a component of the internationally registered oral cholera vaccine Dukoral . We used the bifunctional cross-linking reagent N-succinimidyl 3-(2-pyridyl) -dithio) propionate (SPDP) (Pierce Rockford, Illinois, USA), as recommended by the manufacturer to ensure the coupling of 4-5 peptide residues 336-351 per rCTB pentamer. An aliquot of 500µg CTB in 0.05 M sodium phosphate (2.5mg/ml) at pH 8.6 was incubated with 42µl SPDP for 30 minutes at room temperature and the pH was then adjusted to 7.5. Peptide 336-351 (200mg) was dissolved in 40 ml PBS, mixed with CTB-SSPY and incubated over night at room temperature on a rocking platform. After conjugation, the material was chromatographed on a Sephadex 25 column (Amersham Biosciences, Uppsala, Sweden) and eluted with PBS. The absorbance was recoded at 280 nm, and the protein fractions were collected and pooled. After checking that this material gave a single homogeneous peak it was eluted as a slightly larger protein than unconjugated SPDP-treated rCTB on FPLC. The rCTB-peptide conjugate was sterile-filtered, aliquoted, frozen and then stored. Selected aliquots of the final material were characterized for their sterility, composition, retained binding GM1 ganglioside and also tested for its safety and preventive capacity in the rat uveitis model as reported before being used in the present phase I/II clinical trial.

2. Haematological and biochemical tests

Routine blood indices and chemistry were carried out at every visit of the patients.

3. Immunological investigations

a) Reagents

For analytical purposes HSP65 was prepared from M. bovis as described elsewhere (Mehlert A and Young DB. 1989. Biochemical and antigenic characterisation of the Mycobacterium tuberculosis 71kD antigen, a member of the 70kD heat-shock protein family. Mol. Microbiol. 3:125-130.).

After page 19, please insert the attached paper copy of the sequence listing and renumber the claims pages accordingly.